

Comparison of simultaneously studied high sensitive cardiac troponin T and cardiac troponin I levels in patients diagnosed with acute myocardial infarction

Eurasian Clinical and Analytical Medicine Original Research

Cardiac troponin levels

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Abstract

Aim: The aim of this study was to compare simultaneously studied high sensitive cardiac troponin T (hs-cTnT) and cardiac troponin I (cTnI) level in patients diagnosed with acute myocardial infarction (AMI), undergoing an immediate invasive strategy or an early invasive strategy.

Material and Methods: A total of eighty-five consecutive patients, over eighteen years, diagnosed with non-ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI), in whom hs-cTnT and cTnI, single or serial testing, simultaneously studied and who underwent an immediate invasive strategy or an early invasive strategy, were included in this study. The demographic features of the patients, hemogram, biochemical parameters, hs-cTnT and cTnI level were recorded on admission. The patients were classified into three groups; those with only hs-cTnT elevation (simultaneously cTnI is normal) and those with simultaneous hs-cTnT and cTnI elevation and those whose hs-cTnT and cTnI are simultaneously normal.

Results: There was no patient whose hs-cTnT value was normal when cTnI was elevated. In 34 (40.0%) patients hs-cTnT and cTnI levels were simultaneously elevated, in 33 (38.9%) patients only hs-cTnT level was elevated, in 18 (21.1%) patients hs-cTnT and cTnI levels were normal. 18 (21.1%) patients with normal hs-cTnT and cTnI level had STEMI. While hs-cTnT was high in 100% of NSTEMI patients, 51% had high cTnI. When the three groups were compared, the highest creatinine level ($p=0.013$), the lowest glomerular filtration rate (GFR) level ($p=0.014$), and the highest chronic kidney disease (CKD) ($p=0.010$) rate were observed in only hs-cTnT level elevated group. When the three groups were compared in terms of age and gender, statistically difference was not found between the three groups.

Discussion: Serial hs-cTnT measurements are required to diagnose NSTEMI especially in patients with CKD. Serial cTnI measurements are required to diagnose NSTEMI in normal population because of its low sensitivity. These situation causes delay in diagnosis and treatment. Therefore, cardiac biomarkers with high sensitivity and specificity are needed to diagnose AMI in a shorter time.

Keywords

High Sensitive Cardiac Troponin T, Cardiac Troponin I, Acute Myocardial Infarction

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Introduction

The clinical presentation of AMI is extensive. It ranges from chest pain to cardiac arrest. The leading symptoms with suspected AMI is acute chest discomfort described as pain, pressure, tightness, and burning. Some patients do not have chest pain at the time of admission. Dyspnoea, epigastric pain and pain in the left arm are known chest pain-equivalent symptoms [1]. We use electrocardiography (ECG) and hs-cTnT and cTnI level to diagnose AMI. After the diagnosis of AMI, an invasive strategy is applied according to the type and duration of myocardial infarction. We aimed to compare simultaneously studied hs-cTnT and cTnI level in patients diagnosed with AMI, undergoing an immediate invasive strategy or an early invasive strategy. When hs-cTnT level and cTnI level are studied simultaneously in AMI, both parameters are expected to rise above the 99th percentile of the upper reference limit.

Material and Methods

This study was an observational retrospective study. This research was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the local institutional review board, and waived the requirement for informed consent. The protocol was approved by the local ethics committee (approval date: February 25, 2021 approval number: 2021-32). Blood samples were measured with Roche Diagnostics' 5th generation Cobas e 602 Elecsys analyzer in our biochemistry laboratory. A total of eighty-five consecutive patients, in whom hs-cTnT and cTnI were simultaneously studied and who were admitted to the emergency department (outpatient clinic) or diagnosed with STEMI and NSTEMI while following inpatient clinic and underwent an immediate invasive strategy or an early invasive strategy (invasive coronary angiography, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), between January 1, 2020 and January 1, 2021, were included in this study. Hemogram, biochemical parameters, hs-cTnT and cTnI were studied on admission. Single or serial simultaneous hs-cTnT and cTnI measurements were performed in NSTEMI patients. Since there was no invasive coronary angiography unit in our hospital, the patients were transferred to other hospitals. All demographic and laboratory data were extracted from electronic medical records using a standardized data collection form and patient's file from our hospital archive. Demographic features of the patients such as age, gender, anemia (hemoglobin below 11.7 g/dl) and chronic kidney disease (CKD) were recorded on admission. We measured estimated glomerular filtration rate (eGFR) with Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI). CKD-EPI was calculated electronically using age, gender and race parameters. CKD was defined as eGFR below 60 ml/min/1.73 m². Laboratory findings such as hs-cTn T (normal range was between 0-14 ng/L), cTn I (normal range was between 0-0.16 ng/mL), glucose (normal range was 74-106 mg/dl), hemoglobin (normal range was 11.7-16.0 g/dl), white blood cell (WBC) (normal range was {3,98-10,04 10³/μl}), creatinine (normal range was 0,51-0,95 mg/dl), alanine aminotransferase (ALT) (normal range was 0-35 U/l), C reactive protein (CRP) (normal range was 0-5 mg/l) were recorded on admission.

The patients in whom only hs-cTnT was studied or only cTnI was studied were not included in the study. Patients under eighteen years of age and had a diagnosis of acute pericarditis, acute myocarditis, infective endocarditis, sepsis or malignancy were excluded from the study.

The patients were divided in three groups: Only hs-cTnT elevated group, simultaneously hs-cTnT and cTnI elevated group, simultaneously hs-cTnT and cTnI normal group. There was no patient whose hs-cTnT value was normal while cTnI was high.

All statistical analyses were performed by IBM SPSS statistics version

26 software. The Kolmogorov-Smirnov test was used to determine the normality of the variables. Chi-squared test and Fisher-Freeman-Halton exact test were used to compare qualitative variables. When more than 20% of cells had expected frequencies less than 5, we used Fisher-Freeman-Halton exact test. When no more than 20% of cells with had expected frequencies less than 5, we used chi-squared test. We computed Kruskal Wallis test to compare the median values and one-way ANOVA to compare the mean values. A p value of less than 0.05 was considered as statistically significant. P values were two-tailed.

Results

Between January 1, 2020 and January 1, 2021 a total of 13157 tests (hs-cTnT and cTnI) were performed on 3800 patients with angina and angina equivalent symptoms. The average number of tests per patient was 3.46. 337 patients were diagnosed with AMI and an immediate invasive strategy or an early invasive strategy were performed on the patients in that time. Of these 337 patients, 85 patients in whom hs-cTnT and cTnI were simultaneously studied included in the study. 33 (38.9 %) of them was in the only hs-cTnT elevated group, 34 (40.8 %) of them in the simultaneously hs-cTnT and cTnI elevated group, 18 (21.1 %) of them was in the simultaneously hs-cTnT and cTnI normal group. 31 (36.5 %) of the patients were women and 54 (63.5 %) of the patients were men. The mean age was 65 ±12 (37-88) years. 75 (88.2 %) patients were from outpatient clinic; 10 (11.8 %) patients were from inpatient clinic.

Median glucose level was 130 (105-191) mg/dl, median creatinine level was 1.00 (0.80-1.30) mg/dL, median ALT level was 19 (12-26) U/L, median CRP level was 6.3 (2.3-19.3) mg/L, median WBC level was 9.20 (7.75-10.73)10³/L, median hemoglobin level was 12.7 (10.5-14.5) g/dL, median eGFR level was 70 ±27 (11-115) mL/min/1.73 m². The normal value of hs-cTn T was between 0-14 ng/L, the normal value of cTnI was between 0-0.16 ng/mL. Median hs-cTn T level was 40.72 (15.80-114.25) ng/L, median cTnI level was 0.11 (0.10-0.54) ng/mL. There was anemia in 41 (48.2 %) patients and CKD in 33 (38.8 %) patients. Elevated liver enzymes was found in 10 (11.8 %) patients, elevated CRP was found in 47 (55.3 %) patients and elevated WBC was found in 41 (48.2 %) patients.

In the only hs-cTnT elevated group; the mean age was 67±11 (47-87) years, 21 (63.6 %) of the patients were male and 12 (36.4 %) were female, 30 (90.9 %) patients were from outpatient and 3 (9.1 %) patients were from inpatient clinic. In the simultaneously hs-cTnT and cTnI elevated group the mean age was 66±11 (42-85) years, 23 (67.6 %) of the patients were male and 11 (32.4 %) were female, 28 (82.4 %) patients were from outpatient clinic and 6 (17.6 %) patients were from inpatient clinic. In the simultaneously hs-cTnT and cTnI normal group; the mean age was 59±14 (37-88) years, 10 (55.6 %) of the patients were male and 8 (44.4 %) were female, 17 (94.4 %) patients were from outpatient clinic and 1 (5.6 %) patients were from inpatient clinic.

When the three groups were compared in terms of age, gender and outpatient/inpatient statistically difference was not found between the three groups (p=0.068), (p=0.690), (p=0.505), respectively.

Median creatinine level was 1.00 (0.90-1.60) mg/dl in the only hs-cTnT elevated group, median creatinine level was 1.03 (0.80-1.40) mg/dl in the simultaneously hs-cTnT and cTnI elevated group; median creatinine level was 0.85 (0.70-0.93) in the simultaneously hs-cTnT and cTnI normal group; when the three groups were compared in terms of median creatinine level, creatinine level was lower in the simultaneously hs-cTnT and cTnI normal group which was statistically significant (p=0.013). Median eGFR level was 63 ±29 (11-115) ml/min/1.73 m² in the only hs-cTnT elevated group, median eGFR level was 67 ±24 (13-106) ml/min/1.73 m² in the simultaneously hs-cTnT and cTnI elevated group, median eGFR level was 86 ±23 (21-112) ml/min/1.73 m² in the simultaneously hs-cTnT and cTnI normal group; when the three groups were compared in terms

Table 1. The basic clinical characteristics and laboratory findings of the patients on admission

Variables	Only elevated hs-cTnT n (%) 33 (38.9)	Simultaneously hs-cTnT and cTnI elevated n (%) 34 (40.0)	Simultaneously hs-cTnT and cTnI normal n (%) 18 (21.1)	Total n (%) 85 (100)	p value
Age years mean SD± (min-max)	67±11 (47-87)	66±11 (42-85)	59±14 (37-88)	65 ±12 (37-88)	0.068
Sex Male/Female n (%)	21 (63.6)/12 (36.4)	23 (67.6)/11 (32.4)	10 (55.6)/8(44.4)	54 (63.5)/31 (36.5)	0.690
Glucose mg/dl; median (IQR)	138 (110-181)	135 (105-222)	112 (101-133)	130 (105-191)	0.108
Creatinine mg/dl; median (IQR)	1.00 (0.90-1.60)	1.03 (0.80-1.40)	0.85 (0.70-0.93)	1.00 (0.80-1.30)	0.013
eGFR ml/min/1.73 m ² ; mean SD± (min-max)	63 ±29 (11-115)	67 ±24 (13-106)	86 ±23 (21-112)	70 ±27 (11-115)	0.014
ALT mg/dl; median (IQR)	19 (13-25)	19 (12-28)	19 (12-26)	19 (12-26)	0.99
CRP mg/dl; median (IQR)	5.9 (2.3-19.2)	7.5 (2.9-22.0)	5.5 (1.5-19.8)	6.3 (2.3-19.3)	0.803
WBC 10/L; median (IQR)	9.18 (7.50-12.20)	9.50 (7.98-10.86)	8.55 (6.78-9.99)	9.20 (7.75-10.73)	0.265
Hemoglobin; mg/dl median (IQR)	12.0 (10.2-14.8)	12.7 (10.5-14.4)	13.6 (11.1-14.5)	12.7 (10.5-14.5)	0.643
Anemia n (%)	18 (54.5)	16 (47.1)	7 (38.9)	41 (48.2)	0.556
Chronic kidney disease n (%)	18 (54.5)	13 (38.2)	2 (11.1)	33 (38.8)	0.010
Elevated WBC n (%)	15 (45.5)	19 (55.9)	7 (38.9)	41 (48.2)	0.466
Elevated CRP n (%)	19 (57.6)	20 (58.8)	8 (44.4)	47 (55.3)	0.460
Elevated liver enzyme n (%)	3 (9.1)	5 (14.7)	2 (11.1)	10 (11.8)	0.907
Outpatient/Inpatient n (%)	30 (90.9)/ 3 (9.1)	28 (82.4)/ 6 (17.6)	17 (94.4)/ 1(5.6)	75 (88.2)/ 10 (11.8)	0.505
hs-cTnT ng/L	36.90 (18.86-69.18)	132.50 (53.83-468.00)	6.19 (4.53-9.30)	40.72 (15.80-114.25)	
cTnI ng/mL	0.10 (0.10-0.10)	0.93 (0.37-5.13)	0.10 (0.10-0.10)	0.11 (0.10-0.54)	

of eGFR, median eGFR level was higher in the simultaneously hs-cTnT and cTnI normal group which was statistically significant ($p=0.014$). Median creatinine level was 1.00 (0.90-1.60) mg/dl in the only hs-cTnT elevated group, median creatinine level was 1.03 (0.80-1.40) mg/dl in the simultaneously hs-cTnT and cTnI elevated group; median creatinine level was 0.85 (0.70-0.93) in the simultaneously hs-cTnT and cTnI normal group; median creatinine level was lower in the simultaneously hs-cTnT and cTnI normal group, which was statistically significant ($p=0.013$). CKD rate was 18 (54.5 %) in the only hs-cTnT elevated group, CKD rate was 13 (38.2 %) in the simultaneously hs-cTnT and cTnI elevated group; CKD rate was 2 (11.1 %) in the simultaneously hs-cTnT and cTnI normal group; when the three groups were compared in terms of CKD rate, CKD rate was higher in the only hs-cTnT elevated group, which was statistically significant ($p=0.010$).

When the three groups were compared in terms of following parameters, there was no statistically significant difference between the three groups; median glucose level ($p=0.108$), median ALT level ($p=0.99$), median WBC level ($p=0.265$), median hemoglobin level ($p=0.643$), median hematocrit level ($p=0.527$), anemia ($p=0.556$), elevated liver enzymes ($p=0.907$), elevated WBC ($p=0.466$). The basic clinical characteristics and laboratory findings of the patients on admission are shown in Table 1.

We computed a one-way ANOVA comparing the mean age of three groups (only hs-cTnT elevated, simultaneously hs-cTnT and cTnI elevated group and simultaneously hs-cTnT and cTnI normal group). No significant difference was found among the groups ($F [2,82] = 2.783$, $p = 0.068$).

We computed a one-way ANOVA comparing the mean eGFR of three groups (only hs-cTnT elevated group, simultaneously hs-cTnT and cTnI elevated group and simultaneously hs-cTnT and cTnI normal group). A significant difference was found among the groups ($F [2,82] = 4.537$, $p = 0.014$). Tukey's HSD was used to determine the nature of the differences between the groups. This analysis revealed that simultaneously hs-cTnT and cTnI normal group's mean eGFR was higher (Mean = 86, sd = 23) than the only hs-cTnT positive (Mean = 63, sd = 29) and simultaneously hs-cTnT and cTnI elevated group (Mean = 67, sd = 24).

We computed Kruskal Wallis test to compare the medians of CRP,

glucose, WBC, hemoglobin, ALT, creatinine levels of three groups (only hs-cTnT elevated group, simultaneously hs-cTnT and cTnI elevated group and simultaneously hs-cTnT and cTnI normal group). A significant difference of creatinine levels was found among the three groups ($p=0.013$). Post hoc Tamhane's T2 test was used to determine the nature of the creatinine level difference between the groups. This analysis revealed that simultaneously hs-cTnT and cTnI normal group's median creatinine level was lower (Median = 0.85 IQR = 0.70-0.93) than the only hs-cTnT elevated (Median = 1.00 IQR = (0.90-1.60) ($p=0.020$) and simultaneously hs-cTnT and cTnI positive group (Median=1.03 IQR=0.80-1.40) ($p=0.020$). There was no difference between median creatinine levels of only hs-cTnT elevated and simultaneously hs-cTnT and cTnI elevated group ($p=0.662$).

We computed Chi-square test to compare the three groups in terms of percentage of gender, presence of anemia, high WBC, elevated liver enzyme and CRP level, being presented to the hospital as outpatient or inpatient. Three groups (only hs-cTnT elevated, simultaneously hs-cTnT and cTnI elevated group and simultaneously hs-cTnT and cTnI normal group) were not statistically different in terms of gender ($\chi^2=0.743$, 2 df, $p=0.690$), presence of anemia ($\chi^2=1.175$, 2 df, $p=0.556$), high WBC ($\chi^2=1.528$, 2df, $p=0.466$), elevated liver enzyme ($\chi^2=0.585$, 2 df, $p=0.907$) and CRP levels ($\chi^2=3.575$, 2 df, $p=0.460$), being presented to the hospital as outpatient or inpatient ($\chi^2=1.714$, 2 df, $p=0.505$). A significant difference was found among the three groups ($\chi^2= 9.260$, 2 df, $p= 0.010$) only in terms of presence of CKD. Post hoc analysis after adjusting p values with Bonferoni method, revealed that in patients in simultaneously hs-cTnT and cTnI normal group, presence of CKD was lower than the only hs-cTnT elevated group ($p=0.03$).

Discussion

In our study, we observed that when hs-cTnT and cTnI were studied simultaneously, none of the patients had elevated cTnI level when hs-cTnT level was normal. In addition, hs-cTnT alone was elevated in 40% of all the patients, while the cTnI remained normal. In this study, we observed that hs-cTnT (only hs-cTnT elevated group + with simultaneously hs-cTnT and cTnI elevated group) increased at least one value above the 99th percentile of the upper reference limit in 100 %

of diagnosed with NSTEMI patients. cTnI (simultaneously elevated hs-cTnT and cTnI) increased at least one value above the 99th percentile of the upper reference limit in 51% of diagnosed with NSTEMI patients. In 18 (21.1%) of the patients diagnosed with STEMI, hs-cTnT and cTnI were simultaneously normal. Since the diagnosis of these patients was STEMI, they were diagnosed in less than 1 hour and no additional assays were performed. A significant difference was found among the three groups only in terms of presence of CKD. CKD rate was higher in the only hs-cTnT elevated group which was statistically significant. When the three groups were compared in terms of age and gender, statistically difference was not found between the three groups.

In order to diagnose ACS in patients who apply with these complaints, we need to study ECG and cardiac troponin. The patients with ST elevation >2 mm in ≥ 2 precordial leads, ST elevation >1 mm in ≥ 2 limb leads or new left bundle branch block on the 12-lead electrocardiogram were diagnosed as STEMI and diagnosis of NSTEMI was done according to The Fourth Universal Definition of Myocardial Infarction criteria [2]. Patients with acute chest pain and ST elevation lasting more than 20 minutes are diagnosed with STEMI [3]. Patients with acute chest discomfort but no persistent ST-segment elevation are diagnosed as NSTEMI [4]. The diagnosis of AMI required to meet combination of criteria, namely the detection of an increase and/or decrease of a cardiac biomarker, with at least one value above the 99th percentile of the upper reference limit and at least one of the following:

- (1) Symptoms of myocardial ischaemia
- (2) New ischaemic ECG changes
- (3) Development of pathological Q waves on ECG
- (4) Imaging evidence of loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology
- (5) Intracoronary thrombus detected on angiography or autopsy [1].

In patients with AMI, levels of cardiac troponin rise rapidly (i.e. usually within 1 hour (h) from symptom onset if using high-sensitivity assays) after symptom onset and remain elevated for a variable period of time (usually several days) [1, 4, 5, 6, 7, 8, 9, 10, 11]. It is recommended to use the 0 h/1 h algorithm (best option, blood draw at 0 h and 1 h) or the 0 h/2 h algorithm (second best option, blood draw at 0 h and 2 h). As an alternative, the previous European Society of Cardiology (ESC) 0 h/3 h algorithm should be considered [12]. It is recommended to preferably use hs-cTnT or cTnI in the The Fourth Universal Definition of Myocardial Infarction criteria. Although hs-cTn assays are very sensitive, they are less specific for AMI when using the 99th percentile as a single cutoff level [13]. In many other diseases such as hypertension patients with left ventricular hypertrophy, heart failure, pulmonary embolism, pulmonary artery hypertension, myocarditis, cerebral disease and CKD cardiac troponin level can increase. The negative predictive value (NPV) of hs-cTn assays is 95% for AMI exclusion when patients are tested on arrival at the Emergency department [14]. If this is repeated at 3 h, this rises to nearly 100% [15]. In a previous study using cTnI, the 0/1-h algorithm ruled out 55% of patients (NPV: 100%; 95% CI: 98.8% to 100%), and ruled in 18% of patients (PPV: 76.8%; 95% CI: 67.2% to 84.7%) [15]. In our study we found PPV: 51% using cTnI for ruled in. Therefore, if hs-cTnT is used in patients with CKD, serial hs-cTnT measurements are appropriate to diagnose NSTEMI. In the other study they found that: rule-out sensitivity of hs-cTnT was 97.1% (95% confidence interval [CI]: 94.0%–99.8%), and rule-in specificity was 94.6% (95% CI: 93.4%–95.5%). In our study we found PPV: 100% using hs-cTnT for ruled in [16]. The diagnostic performance of hs-cTn in the assessment of CKD patients presenting with suspected MI was evaluated in the studies of Gonsolus et al., Miller-Hodges et al., Twerenbold et al., Twerenbold et al. compared the diagnostic performance of the 0/1-hour ESC algorithms of rapid rule-in and rule-out in patients with and without renal dysfunction using

both hs-cTnT and cTnI. They found that; the specificity was significantly lower (hs-cTnT: 88.7% vs. 96.5%; hsTnI: 84.4% vs. 91.7%) with sensitivity remaining relatively unchanged (hs-cTnT: 100.0% vs. 99.2%; cTnI: 98.6% vs. 98.5%). They found that the 0/1-hour algorithm the specificity was much lower in patients with renal impairment due to fewer patients fulfilling rule-out criteria (51.3–53.5% vs. 76.1–81.2%) [17]. Similarly, we used the 0/1-0/2h and 0/3h algorithms in patients with CKD in our study to rule-in and rule-out NSTEMI. Therefore, if hs-cTnT is used in patients with CKD, serial hs-cTnT measurements are appropriate to diagnose NSTEMI.

Until now, there has been no study in the literature comparing hs-cTnT and cTnI, which were studied simultaneously in patients who underwent an immediate invasive strategy or an early invasive strategy due to AMI. This study has several limitations. Firstly, the study was a single-center and retrospective study. Secondly, the number of patients participating in the study was small.

Conclusion

Serial hs-cTnT measurements are required to diagnose NSTEMI especially in patients with CKD. Serial cTnI measurements are required to diagnose NSTEMI in normal population because of its low sensitivity. These situation causes delay in diagnosis and treatment. Therefore, cardiac biomarkers with high sensitivity and specificity are needed to diagnose AMI in a shorter time, especially in patients with CKD.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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